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Sponsor/company:	sanofi-aventis	ClinicalTrials.gov Identifier:	NCT00486785
		Study Code:	ALFUS_L_01667
Generic drug name:	Alfuzosin	Date:	06/Feb/2009

Title of the study:	Sexuality And Management of Benign Prostatic Hyperplasia with Alfuzosin 10mg once daily (XATRAL OD 10mg), open, 24-week study SAMBA./ ALFUS_L_01667		
Investigator(s):	Martin Telich Vidal Periferico Sur 3707 – 1180 Col. Heroes de Padierna, C.P. 10700 Mexico D.F. Phone: (+52) 56 52 19 35 Fax: (+52) 51 35 01 69 Email: martintelich@yahoo.com.mx		
Study center(s):	Colombia (13 sites), Ecuador (5 sites), Guatemala (3 sites), México (21 sites)		
Publications (reference):	No publications have been done up to date		
Study period: Date first patient/subject enrolled: 08-Jun-2006 Date last patient/subject completed: 24-Oct-2007		Phase of development: Phase IV	
Objectives:	PRIMARY To assess improvement in MSHQ ejaculation domain from baseline to the end of treatment (Week 24 or premature withdrawal (PW)) with XATRAL 10mg OD. SECONDARY -To evaluate the association between lower urinary tract symptoms (LUTS) severity and sexual disorders, -To compare the improvement in sexual function, urinary symptoms and Quality of Life among the different countries (Colombia, Ecuador, Guatemala, El Salvador, Honduras & Mexico), -To assess the onset of action of XATRAL OD 10mg, -To assess the peak flow rate improvement (Qmax) when Qmax is available, -To assess the safety and the tolerability of XATRAL OD 10mg.		
Methodology:	This study is a non randomized, open label, non – comparative, international, multicentric, with Alfuzosin 10 mg once a day during 24 weeks in males with Benign Prostatic Hyperplasia.		
Number of patients/subjects:	Planned:425	Randomized:	Treated:429
Evaluated:	Efficacy:376	Safety: 429	
Diagnosis and criteria for inclusion:	Male patients aged ≥ 50 years, suffering from moderate to severe Lower Urinary Tract Symptoms (LUTS), defined by an I-PSS total score > 7, and suggestive of symptomatic Benign Prostatic Hyperplasia (BPH), sexually active, who may benefit from treatment with Alfuzosin 10mg OD and having given their written Informed Consent.		
Investigational product: Dose: Administration:	Alfuzosin 10 mg, once a day Oral		
Duration of treatment: 24 weeks		Duration of observation: NA	

Reference therapy:	NA
Criteria for evaluation:	
Efficacy:	Primary: - Mean change from baseline to the end of treatment (Week 24 or premature withdrawal (PW)) in the Male Sexual Health Questionnaire (MSHQ) ejaculation score. The MSHQ has been linguistically validated for each participating country. Secondary: - Mean change from baseline to 4, 12, and 24 weeks of treatment in MSHQ Ejaculation score, - Mean change from baseline to 4, 12 and 24 weeks of treatment in MSHQ erection and satisfaction scores - Mean change from baseline to week 1 in I-PSS total score and sub-scores (objective onset of action), - Onset of action based on patient perception (questionnaire provided to patient at Week 1), - Mean change from baseline to 4, 12 and 24 weeks of treatment in the I-PSS total score and in the Quality of Life.
Safety:	Evaluation of: - Adverse events, vital signs (blood pressure and heart rate), PSA (mandatory at baseline according to the recommendations of the 4th International Consultation on BPH [44] and optional at the end of treatment - Week 24 or PW-) and serum creatinine assessments (optional at baseline and at the end of treatment - Week 24 or PW-).
Statistical methods:	Quantitative data were summarized estimating mean values and standard deviations, as well as medians and ranges. Qualitative data were summarized by frequencies and percentages. All statistical tests were two sided, with a significance level of 5%. 95% confidence intervals were also estimated when needed. Baseline characteristics were described for all countries together, and for each country. The primary efficacy analysis evaluated the impact of treatment on ejaculation, based on the mean of change in the MSHQ ejaculation score from baseline up to the end of the study. The secondary efficacy analysis included: 1) the absolute change and the percentage of change in MSHQ ejaculation score, and in other variables for weeks 4, 12 and 24 of treatment; 2) the onset of action of Alfuzosin 10 mg OD evaluated using the change in the IPSS total score from baseline up to week 1 of treatment, and the patients' perception at week 4; 3) changes in the urinary symptoms evaluated through the mean of change in the total IPSS score and in all IPSS sub-scores from baseline to weeks 4, 12 and 24; 4) a descriptive analysis for the association between the severity of IPSS and the MSHQ sub-scores; 5) the number and percentage of patients with acute urinary retention and BPH surgery; 6) the proportion of patients with improvement in the MSHQ ejaculation score among countries, compared using analysis of covariance; 7) the changes in MSHQ ejaculation score and in the other MSHQ scores, assessed through multivariate analysis; and 8) descriptive statistics for the Qmax results at baseline and at weeks 1, 4, 12 and 24 of treatment. All safety analyses were conducted based on the safety analysis population. Adverse events were classified by system, organ, class (SOC) and preferred term (PT). AE incidence tables were constructed by class, PT and severity. Tables and graphics for blood pressure and heart rate were obtained for patients with data available before and after treatment. Descriptive statistics for PSA and creatinine were obtained at baseline and at week 24.

Summary:	Mean ejaculation score significantly improved from 26.18 (sd 5.37) at baseline to 28.8 (sd 5.79) at end-point (mean (sd) change 2.60 (sd 6.26), median 2.0, with 95% CI between 1.95 and 3.17, p<0.001). Overall, 27.9% of patients showed a 20% or upper improvement in the ejaculation score. I-PSS score significantly improved from 17.24 (sd 5.47) at baseline to 7.14 (sd 5.42) at end-point (mean change 10.09 (6.43), p<0.001). Overall, 368 patients (87.62%) had an improvement of IPSS of at least 3 points. Symptom relief was perceived by most patients (69.3%) from the first week of treatment, 8.87% from the second week and 7.19% from 3-4 weeks. 14.63% were not improved with alfuzosin treatment.

Efficacy results:

Most patients were described as Hispanic (95.3%), mean age was 61.21 years, 23.17% were hypertensive. The mean age for onset of LUTS was 58.07 years. At enrollment, mean Qmax was 13 ml/sec and mean prostate volume was 40.2 ml. Mean MSHQ subscores at enrollment were 9.8 for erection symptom score, 3.5 for bother due to erectile dysfunction (ED), 26 for ejaculation symptom score, 4 for bother due to ejaculatory dysfunction (EjD) and 21.8 for satisfaction.
The mean improvement from baseline in ejaculation score at Week 24 was of 2.46 (95% confidence intervals 1.93-3.18, p<0.001). Overall, 27.93% of patients showed an improvement of at least 20% in ejaculation score at week 24.
Main changes from baseline in the ejaculation score were 2.11 at week 4, 2.43 at week 12 and 2.46 at week 24.
table with results of each MSHQ domain

	Overall population
Ejaculation symptom score - mean value at baseline - mean value at end-point - Mean (sd) change - p - % men with ≥ 20% improvement from baseline	N=376 26.16 (5.37) 28.77 (5.79) 2.60 (6.26) [1.97 – 3.24] < 0.001 27.93%
Bother due to EjD - mean value at baseline - mean value at end-point - Mean (sd) change -p - % men with ≥ 20% improvement	N=376 4.04 (1.13) 4.44 (0.91) 0.39 (1.19) [0.27 – 0.51] < 0.001 35.9%
Erection score - mean value at baseline - mean value at end-point - Mean (sd) change - p - % men with ≥ 20% improvement from baseline	N=376 9.83 (3.25) 11.00 (3.19) 1.17 (3.43) [0.82 – 1.52] < 0.001 39.63%
Bother due to ED - mean value at baseline - mean value at end-point -Mean (sd) change - p - % men with ≥ 20% improvement from baseline	N=376 3.57 (1.28) 4.15 (1.02) 0.59 (1.27) [0.46 – 0.71] < 0.001 44.41%
Satisfaction score - mean value at baseline - mean value at end-point -mean (sd) change - p - % men with ≥ 20% improvement from baseline	N=376 21.82 (6.43) 24.59 (5.94) 2.77 (6.04) [2.16 – 3.38] < 0.001 32.18%

Differences in scores were equal to 20% or superior when compared to baseline in 39.71% for the erection score, 43.58% for the erection problems score, 27.12% for the ejaculation score, 35.35% in the ejaculation problems score and 31.48% in satisfaction score.

When evaluating I-PSS at week 24 there was a reduction of 3 or more points in 88.47% of patients and a reduction of less than 3 points in 4.29%. The changes in I-PSS were noticeable since the very first week, with 67.14% of the population having a reduction in 3 or more points in week 1, 80.15% in week 4 and 88.69 in week 12. There was improvement, according to the patient's perception in 69.3% in the first week, 8.87% in the second week, 7.19% in the 3-4 weeks and no improvement in 14.63%.

When evaluating I-PSS at week 24, 330 patients (88.47%) had an improvement of IPSS of at least 3 points. The changes in I-PSS were noticeable since the very first week, with 67.14% of patients having an improvement in IPSS of at least 3 points at week 1, 80.15% at week 4 and 88.69 at week 12. Symptom improvement was perceived by the patient in 69.3% within the first week, 8.87% within the second week, 7.19% within the 3-4 weeks and 14.63% had no improvement in LUTS.

Description of changes in I-PSS

	n	%
Week 1		
Reduction in 3 or more points	282	67.14
Reduction of less than 3 points	59	14.05
Unchanged	30	7.14
Increase in less than 4 points	28	6.67
Increase in 4 or more points	21	5.00
Week 4		
Reduction in 3 or more points	327	80.15
Reduction of less than 3 points	36	8.82
Unchanged	9	2.21
Increase in less than 4 points	21	5.15
Increase in 4 or more points	15	3.68
Week 12		
Reduction in 3 or more points	353	88.69
Reduction of less than 3 points	15	3.77
Unchanged	6	1.51
Increase in less than 4 points	15	3.77
Increase in 4 or more points	9	2.26
Week 24 or premature withdrawal		
Reduction in 3 or more points	368	87.62
Reduction of less than 3 points	19	4.52
Unchanged	10	2.38
Increase in less than 4 points	9	2.14
Increase in 4 or more points	14	3.33

Description in Qmax

Qmax	n	Mean	SD	Median	Range
Baseline	104	12.94	6.65	10.90	1.00 - 35.00
Week 1	40	13.85	5.40	11.95	5.00 - 28.60
Week 4	40	15.81	7.12	14.00	4.80 - 33.30
Week 12	33	14.71	7.04	13.10	5.00 - 32.30
Week 24 or premature withdrawal	69	17.07	7.73	15.00	3.30 - 39.20

Safety results:

There were treatment emergent AEs in 15.15% of patients, and 3 serious events, with no death. Treatment was discontinued in 11 (2.56%) patients due to adverse events.

The detail for serious adverse events are in the following table:

Patient	Date	Reason for SAE	Diagnostic or Main Symptom	Action with study medication	Relation to study	Outcome
10105026	28/05/2007	Require hospitalization	Supropubic surgery of prostate	Discontinuation	Excluded	Recovered
60102008	08/12/2006	Require hospitalization	Acute myocardial infartion	None	Excluded	Recovered with sequalae
60106012	24/05/2007	Require hospitalization	Urinary acute retention	Discontinuation	Excluded	Recovered

The details for adverse events are in the following table:

Adverse Event	Number of patients
Dizziness	12
Postural hypotension / hypotension	1
Malaise	3
Syncope	5
Erectile dysfunction	1
Ejaculatory dysfunction	1

Date of report: 06-Oct-2008